Research Article
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Profile of Intravenous Preparation Mixing in Patients at the Regional General Hospital's Intensive Care Unit Abdoel Wahab Sjahranie Samarinda

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Abstract: Compatibility is one of the quality characteristics of intravenous (IV) preparations that influences the effectiveness of patient therapy in the intensive care Unit (ICU). This study aimed to determine the compatibility profile of IV medication formulations given to ICU patients. This prospective observational research was undertaken on patients in the ICU of a private hospital in Samarinda. The data on the intravenous combination of drugs were compared in this study utilizing the ASHP Injectable Drug Information literature 21st edition, Injectable drug guide, and Manual Book. Injectable Drug Mixing was published in 2009 as a resource for determining the compatibility of intravenous formulations. Using certain criteria, combinations of intravenous medicines and their solvents are classed as compatible (C), incompatible (I), and unknown (U). The ICU had 25 patients, 15 of whom were male, and 10 of them were female. There is no mixing of drug compounds containing incompatible solvents. All drugs were carried out with 100% compatible solvents. The limited information related to the compatibility and stability of these intravenous preparations encourages continuous monitoring of the patient's condition and drug levels.

Introduction

One of the mixings of sterile preparations carried out in the hospital is IV preparations. IV preparations are sterile preparations that are injected directly into blood vessels. The preparation is a solution, while suspension or emulsion are not allowed as it will clog the veins. The volume of intravenous injections generally ranges from 1-10 ml. Intravenous injection should be pyrogen-free and contain a non-irritating liquid that can mix with water. Intravenous injection solutions must be clear and free of deposits or solid particles, as they can clog capillaries and cause death.

Compatibility is a condition of mixing multiple medicinal materials with solvents with no signs of chemical interaction. However, a potential problem called incompatibility can occur during mixing and administering intravenous preparations. Incompatibility is an undesirable reaction that can change the chemical, physical, or therapeutic stability of a drug preparation or so-called unmixed condition (1). Therefore, the mixing of intravenous preparations needs careful evaluation to prevent physical and chemical incompatibility. The process of mixing intravenous preparations is often carried out in patients in the intensive care unit (ICU) because ICU patients have a higher risk of experiencing medication errors (ME) when compared to other inpatients. The conditions of patients treated in the ICU are generally unstable, and they generally receive therapy through the intravenous route (2). Drug administration via the intravenous route provides a faster therapeutic effect with an optimum dose adjusted according to the patient's condition.

The limited information on the compatibility and stability of intravenous preparations encourages continuous monitoring of the patient's condition and

drug levels. Based on these reasons, we are interested in conducting research in the Abdoel Wahab Sjahranie Samarinda Regional General Hospital ICU and aim to identify the profile of the mixing of intravenous preparations.

Methodology

Research Type

This research is a descriptive observational with a cross-sectional research design by taking population data or intravenous dosage samples only once simultaneously. Data collection is carried out on a prospective basis.

Research Population

The study population was mixed intravenous preparations in the intensive care unit (ICU) room of the Abdoel Wahab Sjahranie Samarinda Regional General Hospital.

Research Sample

The sample used was all populations in the intensive care unit (ICU) room of the Abdoel Wahab Sjahranie Samarinda Regional General Hospital.

Population Criteria

Patient criteria were split into the inclusion criteria and the exclusion criteria. Inclusion criteria consisted of all observed intravenous preparation mixing processes classified into the 4 most widely used drugs for Abdul Wahab Sjahranie Samarinda Hospital ICU patients. Exclusion criteria consisted of mixing intravenous preparations, classified into the 4 most widely used drugs for ICU patients at Abdul Wahab Sjahranie Samarinda Hospital, but not all of them were observed.

Data Analysis Technique

Data were analyzed with the measures carried out that were included in the data collection, classification of data processing, and making conclusions by comparing written provisions in the literature. The results of the mixed profile analysis are expressed in the form of a percentage value (%) calculated with the formula Percentage=(Number of compatible intravenous mixture preparations)/(Total Mixing) x100 %. Data was collected by looking at the patient's medical record (RM). The data were the patient's name, gender (Male and Female), age, diagnosis, and medication given. The results of the analysis of intravenous drug mixtures are classified into compatible (K), incompatible (I), and unknown (U). The references used to classify these intravenous drugs are ASHP Injectable Drug Information edition 21 and injectable drug guide.

Results and Discussion

Based on the results of observations of patient characteristics during this study period, 25 patients met the inclusion criteria from July - August 2022. The majority of patients in the ICU of the Abdoel Wahab Sjahranie Regional General Hospital in Samarinda City are men (n=15), and the most diagnosed disease was typhoid (n=10).

Patient Demographic Data

The patients in the ICU of the Abdoel Wahab Sjahranie Regional General Hospital, Samarinda City, were 15 patients, and the most diagnoses obtained by typhoid disease, as many as 10 patients, can be seen in Table 1.

Table 1. Patient demographic data.

Demographic Data	Amount & Percentage (n=25) patient
Gender	
Male	15 (57%)
Female	10 (43%)
Diagnosis	
Typhoid	10 (58%)
Pneumonia	7 (30%)
Sepsis	5 (8%)
Meningitis	4 (4%)

This study used 200 mixings conducted in the ICU room of the Abdoel Wahab Sjahranie Regional General Hospital with 26 patients. Patient characteristics and diagnoses are presented in Table 1. Gender is divided into 2 categories. The analysis of the mixing profile produces a percentage value, and a result of 100% is achieved.

Fauzi I. (2020) conducted research using the chi-square method to analyze data, with the p-value used as the basis for interpretation. The obtained result of 0.776, which was greater than 0.05, indicated a lack of statistically significant association between the sex of the patient and the therapy received (3). This can be interpreted to mean that gender has no correlation or relationship with the incidence of therapy in the patient; in other words, the sex of the patient does not determine how big the incidence is in the patient's therapy. Based on the study results, the most frequent diagnosis was typhoid disease, and the second most common diagnosis was pneumonia, followed by other diseases.

List of Mixed Drugs

Based on the results of the observation of the percentage of the drug list carried out by mixing intravenous preparations in the ICU room of the Abdoel Wahab Sjahranie Regional General Hospital can be seen in Table 2.

According to the Ministry of Health (2009), the preparation and mixing of parenteral preparations must be carried out by pharmacists or pharmaceutical

personnel trained under the responsibility and supervision of hospital pharmacy installation pharmacists (4). However, at RSUD Abdoel Wahab Sjahranie, we observed that the preparation and mixing of drugs were carried out by nurses in the ICU room who were competent and attended dispensing training for sterile preparations. This is due to the absence of pharmacists or pharmaceutical technical personnel.

The number of nursing personnel working in the ICU room was 34. For the compounding process in the ICU room, only 1 nurse was involved. Table 2 shows that the most frequently compounded drugs before administration are ceftriaxone (40%), omeprazole (35%), meropenem (15%), and tramadol (10%), as indicated by their high rankings. Based on the results of observations, the most frequently used drug was ceftriaxone.

Table 2. List of drugs mostly mixed.

No.	Drug Name	Dosage Form of The Drug	Dosage Strength	Amount	Percentage (100%)
1	Ceftriaxone	Vial	1 g	80	40
2	Omeprazole	Vial	40 mg	70	35
3	Tramadol	Ampoule	100 mg	30	15
4	Meropenem	Vial	1 g	20	10
Total				200	100

Visual Observation Results

The results of visual observations (physical quality test of mixing intravenous preparations) are given in Table 3.

Table 3. Visual observation of intravenous preparations.

No.	Drug Name	Parameters observed	Information according to the literature	Observations	Amount	Percentage (%)
1	Ceftriaxone 1 g	Solution Color	Light yellow	Light yellow	80	40
		Lucidity	The solution must be clear and particle-free	Clear, particle-free solution		
2	Omeprazole 40 mg	Solution Color	Colorless	Colorless	70	35
		Lucidity	The solution must be clear and particle-free	Clear, particle-free solution		
3	Tramadol 100 mg	Solution Color	Colorless	Colorless	30	15
		Lucidity	The solution must be clear and particle-free	Clear, particle-free solution		
4	Meropenem 1 g	Solution Color	Colorless	Colorless	20	10
		Lucidity	The solution must be clear and particle-free	Clear, particle-free solution		
Total					200	100

Table 4. Types of solvents used in the mixing.

No.	Drug Name	Dosage form of the drug	Strength of medicinal preparations	Types of Solvents according to the literature	Observations
1	Ceftriaxone	Vial	1 g	*Water for injection*	*Water for injection*
2	Omeprazole	Vial	40 mg	*Water for injection*	*Water for injection*
3	Tramadol	Ampoule	100 mg	NaCl 0.9 %	NaCl 0.9 %
4	Meropenem	Vial	1 g	NaCl 0.9 %	NaCl 0.9 %

Visual observations can be made with the help of dark backgrounds. Observations were made to see physical discrepancies, including deposition, particles, fog, and changes in color, smell, and gases. The visual observations showed that Ceftriaxone, Meropenem, Omeprazole, and Tramadol showed clear, clean, bright results with no sediment or discoloration. From the results, it can be concluded that mixing the four drugs with water for injection and NaCl 0.9% was compatible.

Drug Preparation Procedure

The drug preparation procedure is given in Table 4. The mixing technique at the hospital was not following the standard because, based on the observation results, the vial was shaken while the needle stayed inside the vial. However, due to limited facilities and infrastructure, there was no LAF in the mixing room. The needle can be left in the vial during the mixing process to prevent syringe contamination. Then, a J-Motion movement was sufficient to dissolve the powder until the entire powder in the vial was dissolved (Ministry of Health, 2009). This movement aims to prevent the presence of powder attached to the rubber vial, which causes the drug not to dissolve completely. It is recommended to rub at a 90° angle in this position. There is increased contact between the substance and the solvent, thereby improving the substance's solubility. Based on the observation results, several solvents are used in mixing based on the solvent of each type of drug to be dissolved.

In the Injectable Drug Guide literature (2012) and the Injectable Drug Guidelines and Cytostatics (2009), ceftriaxone and omeprazole are compatible with 0.9% NaCl but based on the results of research, Ceftriaxone is compatibly dissolved with water for injection, omeprazole is compatibly dissolved with water for injection, tramadol is compatibly dissolved with NaCl 0.9%, and compatible meropenem is dissolved with NaCl 0.9% it can be concluded that the solvent is following the ASHP Injectable Drug literature Information 21st edition (5).

pH Measurement Results

The pH measurement results are given in Table 5. The pH measurement of the mixture was carried out because the mixture was said to be incompatible if the mixture produced a change in pH from the initial reading to the next reading or the final pH test. Such changes in the pH value that do not correspond to the literature may indicate active changes in the mixture that are chemically unstable. pH measurements can be carried out with the help of a universal pH indicator tool.

Table 5. pH of intravenous preparations.

No.	Drug Name	pH according to the literature	Sample pH	Percentage (%)
1	Ceftriaxone 1 gram	6,7 (6-8)	6	40
2	Omeprazole 40 mg	8,8-10	9	35
3	Tramadol 100 mg	6-7	7	15
4	Meropenem 1 gram	4,0-6,0	6	10
Total				100

According to Housman et al. (2011), many important components must be considered in mixing parenteral preparations. The pH of the drug will impact the occurrence of incompetence (6). Chemical incompatibility describes how the chemical degradation of one or more mixed drugs causes toxicity or therapeutic inactivation. Degradation is not always directly observable. A specific pH value or a narrow range of pH values is necessary to maintain the stability of the drug after mixing. It can be concluded that the samples' pH follows the pH in the literature.

Compatibility and Incompatibility

Compatibility is one of the determining factors for the quality of intravenous preparations (IV), which impacts the success of therapy for ICU patients. The results of mixing obtained from Ceftriaxone, Omeprazole, Tramadol, and Meropenem suggest no changes (2). Physical incompatibility that can occur from the results of observations includes the formation of white particles that float in the liquid, become cloudy after mixing, and the presence of foam and gas after mixing.

The study findings indicate that the physical characteristics of parenteral drug preparations Cefriaxone, Omeprazole, Tramadol, and Meropenem can be determined by visual tests for discoloration and turbidity. The drugs were physically stable, with no color changes or cloudiness. Any incompatibilities were identified as deposits, loss of active substances, fog formation, and drug adsorption on packaging materials, which did not occur during the mixing process based on the research results. The results of chemical observations can be known from the changes in pH that occurred during the observation time. The mixing of Ceftriaxone, Omeprazole, Tramadol, and Meropenem is compatible. Both the solvent and also the volume used are appropriate.

This study divided IV preparation into small-volume parenteral preparation and large-volume parenteral preparation. Parenteral preparations with small volumes are defined as sterile drugs in less than 100 ml containers. This definition is based on the fact that in this study, the drug preparations of ceftriaxone 1 g and omeprazole 40 mg were dissolved in 10 ml syringes with water for injection as the solvent. The parenteral preparations of small volumes are pharmaceutical products consisting of organic and inorganic chemicals in solution, suspensions, emulsions, freezing dry products, or sterile powders. Biological products from biological sources include vaccines, toxoids, and biological extracts. Meanwhile, in this study, large-volume parenteral preparations are sterile liquid preparations containing drugs packaged in containers of 100 ml or more and intended for humans, such as in infusion bag infusion containers in tramadol drug preparations of 100 mg/2 ml and meropenem 1 g dissolved with 0.9% NaCl in the infusion bag.

Conclusion

Based on the results of the research conducted in June-August 2022 in the ICU room of the Abdoel Wahab Sjahranie Samarinda Regional General Hospital, the mix of intravenous preparations followed the literature with a percentage result of 100%, and no incompatibility events were found in the patients of the ICU room. The stability of the mixing results was supported by pH measurements, as there was no difference in the pH value measured in the pH range based on the literature. We also recommend that only pharmacists be responsible for mixing IV preparations in clinical settings.

Declarations

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Conflict of Interest

The authors declare no conflicting interest.

Data Availability

The unpublished data is available upon request to the corresponding author.

Ethics Statement

Not applicable.

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Not applicable.

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